


PATENT

Attorney Docket No.: A-64411-2/RFT/RMS/RMK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: ) Examiner: Unknown  
)  
MEADE, et al. ) Group Art Unit: 1656  
)  
Serial No.: To be assigned )  
)  
Filed: Herewith ) "EXPRESS MAIL" MAILING LABEL  
) NUMBER EL 758 643 073 US  
) DATE OF DEPOSIT August 3, 2001  
) I HEREBY CERTIFY THAT THIS PAPER OR FEE IS  
For: METALLIC SOLID SUPPORTS ) BEING DEPOSITED WITH THE UNITED STATES  
MODIFIED WITH NUCLEIC ) POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO  
ACIDS ) ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE  
) DATE INDICATED ABOVE AND IS ADDRESSED TO:  
\_\_\_\_\_) BOX PATENT APPLICATION, ASSISTANT  
COMMISSIONER FOR PATENTS, WASHINGTON, DC  
20231.  
  
TYPED NAME Darryl Kriner  
SIGNED 

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents  
Washington, DC 20231

Sir:

Prior to examination of the above identified application, please amend as follows:

In the Claims:

Please cancel claim 1 without prejudice or disclaimer.

Please add the following new claims:

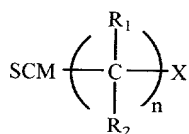
--15. An array of nucleic acids comprising a solid support having a plurality of regions,  
each region comprising an electrode comprising a self-assembled mixed monolayer  
comprising:

- a) blocking moieties, having a first end attached to said electrode, wherein  
said blocking moieties shield nucleic acids from said electrode; and

- b) at least one modified nucleic acid, comprising a nucleic acid and a linker moiety having a first and second end, wherein said first end of said linker is attached to said electrode and said second end is attached to said nucleic acid;
- c) wherein said blocking moieties, together with said modified nucleic acid form a self assembled monolayer; and,

wherein at least two different regions comprise different nucleic acids.

16. An array according to claim 15 wherein said first end of said blocking moieties is attached to said electrode via a sulfur linkage.
17. An array according to claim 15 wherein said first end of said linker is attached to said electrode via a sulfur linkage.
18. An array according to claim 15, 16 or 17 wherein each electrode comprises gold.
19. An array according to claim 15 wherein said blocking moieties have the formula:



wherein

SCM is a sulfur-containing moiety, wherein said sulfur containing moiety is attached to said electrode;

$R_1$  and  $R_2$  are independently selected from the group consisting of hydrogen and substituent groups;

$n$  is an integer from 3 to 50; and

$X$  is a terminal group.

20. An array according to claim 19 wherein  $R_1$  and  $R_2$  are hydrogen.

21. An array according to claim 15 wherein said blocking moieties comprise alkyl.

22. An array according to claim 19, 20 or 21 wherein  $n$  is  $\geq 6$ .

23. An array according to claim 15 wherein said blocking moiety is a branched molecule.

24. An array according to claim 15 wherein said linker moiety is a straight chain alkyl group.

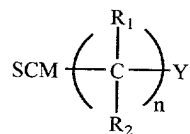
25. A straight chain alkyl group according to claim 24 wherein said chain ranges from 1 to 20 carbon atoms.

26. An array according to claim 15 wherein at least two of said blocking moieties are different.

27. An array according to claim 15 wherein at least one of said blocking moieties is a branched molecule.

28. An array according to claim 26 or 27 wherein at least one of said blocking moieties is an alkyl group.

29. An array according to claim 15 wherein said linker moiety has the formula:



wherein

SCM is a sulfur-containing moiety, wherein said sulfur containing moiety is attached to said electrode;

R<sub>1</sub> and R<sub>2</sub> are independently selected from the group consisting of hydrogen and substituent groups;

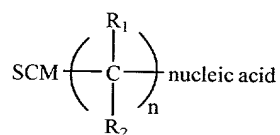
n is an integer from 3 to 50; and

Y is the point of attachment for a nucleic acid.

30. An array according to claim 29 wherein said linker moiety is a straight chain alkyl group.

31. A straight chain alkyl group according to claim 30 wherein said chain ranges from 1 to 20 carbon atoms.

32. An array according to claim 15 wherein said modified nucleic acids have the formula:



wherein

SCM is a sulfur-containing moiety, wherein said sulfur containing moiety is attached to said electrode;

R<sub>1</sub> and R<sub>2</sub> are independently selected from the group consisting of hydrogen and substituent groups; and

n is an integer from 3 to 50.

33. An array according to claim 32 wherein R<sub>1</sub> and R<sub>2</sub> are hydrogen.

34. An array according to claim 29, 32 or 33 wherein n is ≥6.

35. An array according to claim 15 wherein said blocking moiety comprises a phosphorus-containing moiety.

36. An array according to claim 15 wherein said nucleic acid is attached to said linker at a 2' position of a ribose.

37. An array according to claim 15 wherein said nucleic acid is attached to said linker at a 3' position of a ribose.

38. An array according to claim 15 wherein said nucleic acid is attached to said linker at a base of said nucleic acid.

39. An array according to claim 15 wherein said nucleic acid is attached to said linker at a phosphate linkage of said nucleic acid.

40. An array according to claim 15 wherein said solid support is glass.

41. An array according to claim 15 wherein said solid support is plastic.

42. A method of detecting a mismatch, said method comprising adding a target nucleic acid to an array of probe nucleic acids comprising a solid support having a plurality of regions, each region comprising an electrode comprising a self-assembled mixed monolayer comprising:

- a) blocking moieties, having a first end attached to said electrode, wherein said blocking moieties shield nucleic acids from said electrode;
- b) at least one modified nucleic acid comprising a probe nucleic acid and a linker moiety having a first and second end, wherein said first end of said linker is attached to said solid support and said second end is attached to said nucleic acid;
- c) adding an agent that distinguishes between single- and double-stranded nucleic acids;

wherein at least two different regions comprise different probe nucleic acids;  
under conditions wherein at least one of said probe nucleic acids and said target nucleic acid will hybridize to form a hybridization complex.

43. A method according to claim 42 wherein said agent is an intercalating agent.

44. A method of detecting a mismatch, said method comprising adding a target nucleic acid to an array of probe nucleic acids comprising a solid support having a plurality of regions, each region comprising an electrode comprising a self-assembled mixed monolayer comprising:

- a) blocking moieties, having a first end attached to said electrode, wherein said blocking moieties shield nucleic acids from said electrode;
- b) at least one modified nucleic acid comprising a probe nucleic acid and a linker moiety having a first and second end, wherein said first end of said linker is attached to said solid support and said second end is attached to said nucleic acid;
- c) wherein said blocking moieties, together with said modified nucleic acid form a self assembled monolayer;

wherein at least two different regions comprise different probe nucleic acids;  
under conditions wherein at least one of said probe nucleic acids and said target nucleic acid will hybridize to form a hybridization complex.

45. A method according to claim 44 wherein said target nucleic acid is labeled.

46. A method according to claim 42 or 44 wherein said blocking moiety is a branched molecule.

47. A method according to claim 42 or 44 wherein at least two of said blocking moieties are different.

48. A method according to claim 42 or 44 wherein said blocking moiety is a straight chain alkyl group.

49. A method according to claim 42 or 44 wherein said linker moiety is a straight chain alkyl group.

50. An alkyl chain according to claim 48 or 49 wherein said chain ranges from 1 to 20 carbon atoms.--

#### **REMARKS**

Claim 1 has been cancelled. Claims 15-50 are newly added. Support for new claim 15 is found on page 15, line 21 through page 16, line 6. Support for new claims 16-41 is found in allowed claims 16-41. Support for new claims 42 and 43 is found on page 25, line 20 through page 26, line 9. Support for new claim 44 is found in allowed claim 42 and on page 15, line 21 through page 16, line 6. Support for new claims 45-50 is found in allowed claims 43-48.

Attached hereto is a marked-up version of the changes made to the claims by the "Restriction and Amendment". The attached page is captioned **"Version with markings to show changes made."**

The Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-64411-2/RFT/RMS/RMK).



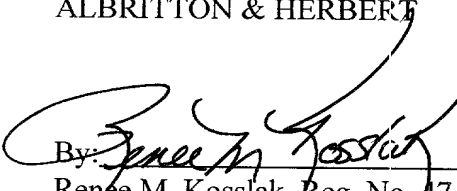
Please direct any calls in connection with this application to the undersigned at

(415) 781-1989.

Dated: 8/3/01

Respectfully submitted,

FLEHR, HOHBACH, TEST,  
ALBRITTON & HERBERT

By:   
Rence M. Kossiak, Reg. No. 47,717 for  
Robin M. Silva, Reg. No. 38,304

Four Embarcadero Center - Suite 3400  
San Francisco, California 94111-4187  
Tel.: (415) 781-1989  
Fax: (415) 398-3249

1057447.RMK

**“VERSION WITH MARKINGS TO SHOW CHANGES MADE”**

In the Claims:

Claim 1 has been cancelled